

Applicants: Bradley *et al.*
U.S.S.N. 09/853,343

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (currently amended) A composition comprising a nucleic acid or an analog or mimetic thereof, a polysaccharide or an analog or mimetic thereof, a lipid or an analog or mimetic thereof, a peptidomimetic or a nonbiopolymeric small molecule modified by reaction with a compound having the formula: R₁ — X — R₂, wherein R₁ comprises a cyclic ether group or an amino group, R₂ comprises an alkoxysilane group soluble in solution and X comprises a moiety for linking the cyclic ether group or the amino group to the alkoxysilane group.
2. (previously amended) The composition of claim 1, wherein the cyclic ether comprises a compound comprising an epoxide group.
3. (previously amended) The composition of claim 2, wherein the epoxide comprises ethylene oxide.
4. (previously amended) The composition of claim 1, wherein the cyclic ether comprises an oxirane group.
5. (previously amended) The composition of claim 1, wherein the cyclic ether comprises a compound comprising an aromatic hydrocarbon epoxide group.
6. (currently amended) The composition claim 1, wherein the R₁ group reacts with the nucleic acid or an analog or mimetic thereof, the polysaccharide or an analog or mimetic thereof, the lipid or an analog or mimetic thereof, or the peptidomimetic.
7. (previously amended) The composition of claim 6, wherein the R₁ group is covalently bound to the nucleic acid or an analog or mimetic thereof, the polysaccharide or an analog or mimetic thereof, the lipid or an analog or mimetic thereof, the peptidomimetic or the small molecule.
8. (previously amended) The composition of claim 1, wherein the composition comprises a modified peptidomimetic.
9. (previously amended) The composition of claim 1, wherein the composition comprises a modified polysaccharide or an analog or a mimetic thereof.
10. (previously amended) The composition claim 1, wherein the composition comprises a modified small molecule.

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12. (previously amended) The composition of claim 1, wherein the composition comprises a modified nucleic acid or an analog or mimetic thereof.
13. (previously amended) The composition of claim 12, wherein the nucleic acid comprises a DNA or an RNA.
14. (previously amended) The composition of claim 12, wherein the nucleic acid reacts with the R₁ group at its 5' end.
15. (previously amended) The composition of claim 12, wherein the nucleic acid is an oligonucleotide.
16. (previously amended) The composition of claim 12, wherein the nucleic acid comprises a telomeric structure.
17. (previously amended) The composition of claim 12, wherein the nucleic acid comprises a chromatin structure.
18. (previously amended) The composition of claim 1, wherein cyclic ether comprises an epoxide group and the alkoxy silane is —Si(OCH₃)₃, —Si(OC₂H₅)₃, —Si(OCH₃)H₂, —Si(OCH₃)(CH₃)₂, or —Si(OCH₃)₂CH₃.
19. (previously amended) The composition of claim 1, wherein cyclic ether comprises an epoxide group and the compound is 3-glycidoxypolytrimethoxysilane (GPTS).
20. (previously amended) The composition of claim 1, wherein the R₁ amino group comprises a primary amino group.
21. (currently amended) The composition of claim 1, wherein R₁ comprises an amino group and the alkoxy silane is selected from the group consisting of —Si(OCH₃)₃, —Si(OC₂H₅)₃ and
$$\begin{array}{c} \text{R}_1 \\ | \\ -\text{Si}-\text{R}_2 \\ | \\ \text{R}_3 \end{array}$$
wherein R₁, R₂ and R₃ are selected from the group consisting of —H, —CH₃, —OCH₃, and —OC₂H₅, and provided that at least one of R₁, R₂ or R₃ is either a group and the compound comprises 3-aminopropyltriethoxysilane.

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23. (previously amended) An article of manufacture comprising an arrayed plurality of biological molecules covalently bound to a surface,

wherein before attachment to the surface, the biological molecules are modified by reaction with a compound having the formula: R₁—X—R₂, wherein R₁ is a cyclic ether group or an amino group, R₂ is an alkoxysilane group and X is a moiety chemically suitable for linking the cyclic ether group or the amino group to the alkoxysilane group, and upon attachment to the surface the modified biological molecules are covalently bound to the surface;

wherein each biological molecule is attached to the surface on at least one discrete and known location to form a cluster of substantially identical biological molecules.

24. (original) The article of manufacture of claim 23, wherein the surface is glass.

25. (original) The article of manufacture of claim 23, wherein the surface is mica or quartz.

26. (original) The article of manufacture of claim 23, wherein the surface is a metal oxide surface.

27. (original) The article of manufacture of claim 23, wherein the metal oxide surface is selected from the group consisting of an alumina (Al₂O₃), a titania (TiO₂), a SnO₂, a RuO₂, or a PtO₂.

28. (original) The article of manufacture of claim 23, wherein the surface is selected from the group consisting of a polystyrene, a polyester, a polycarbonate, a polyethylene, a polypropylene, and a nylon.

29. (original) The article of manufacture of claim 23, wherein the modified biological molecules are covalently bound to the surface via the R₂ group.

30. (original) The article of manufacture of claim 23, wherein the biological molecules are derived from a human.

31. (original) The article of manufacture of claim 23, wherein the biological molecules are derived from a mouse.

32. (original) The article of manufacture of claim 23, wherein the biological molecules comprise a nucleic acid, or an analog or a mimetic thereof.

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34. (original) The article of manufacture of claim 32, wherein the nucleic acid is an oligonucleotide.

35. (original) The article of manufacture of claim 23, wherein the biological molecule comprises a polypeptide, a peptide, or a peptidomimetic.

36. (original) The article of manufacture of claim 23, wherein the biological molecule comprises a polysaccharide, or an analog or a mimetic thereof.

37. (original) The article of manufacture of claim 23, wherein the biological molecule comprises a lipid, or an analog or a mimetic thereof.

38. (original) The article of manufacture of claim 23, wherein the biological molecule comprises a small molecule.

39. (original) The article of manufacture of claim 32, wherein the nucleic acid reacts with the R₁ group at the 5' end.

40. (original) The article of manufacture of claim 32, wherein the nucleic acid comprises a plurality of fragments of a genomic nucleic acid.

41. (original) The article of manufacture of claim 40, wherein the genomic nucleic acid is derived from a normal cell.

42. (original) The article of manufacture of claim 40, wherein the genomic nucleic acid is derived from a cell suspected of having a chromosomal defect or abnormality.

43. (original) The article of manufacture of claim 42, wherein the cell suspected of having a chromosomal defect or abnormality is a tumor cell.

44. (original) The article of manufacture of claim 40, wherein the fragments of genomic nucleic acid further comprise a cloning vehicle.

45. (original) The article of manufacture of claim 44, wherein the cloning vehicle comprises a bacterial artificial chromosome (BAC).

46. (original) The article of manufacture of claim 44, wherein the cloning vehicle comprises a plasmid, a cosmid, a bacteriophage P1-derived vector (PAC), a yeast artificial chromosome (YAC) or a mammalian artificial chromosome (MAC).

47. (original) The article of manufacture of claim 32, wherein the nucleic acid

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48. (original) The article of manufacture of claim 40, wherein the fragments of genomic nucleic acid comprise sequences representing at least one substantially complete chromosome or at least one defined section of a chromosome.

49. (original) The article of manufacture of claim 40, and each genomic nucleic acid fragments has been mapped to a known location on a chromosome.

50. (original) The article of manufacture of claim 40, wherein genomic nucleic acid fragments have a size no more than about 1.2 megabase.

51. (original) The article of manufacture of claim 50, wherein genomic nucleic acid fragments are no more than about 1.0 megabase in size.

52. (original) The article of manufacture of claim 23, wherein each cluster consists of between about 10 and 200 substantially identical copies of a biological molecule.

53. (original) The article of manufacture of claim 23, wherein the surface consists of less than about 400 clusters per square centimeter.

54. (original) The article of manufacture of claim 23, wherein each cluster is about 50 microns in diameter or smaller.

55. (original) The article of manufacture of claim 54, wherein each cluster is about 25 microns in diameter or smaller.

56. (original) An article of manufacture comprising an array of cloned genomic nucleic acid fragments representing a defined subsection of or a substantially complete chromosome,

wherein before attachment to the surface, the cloned fragments are modified by reaction with a compound having the formula: R₁—X—R₂, wherein R₁ is an epoxide group, R₂ is an alkoxysilane group and X is a moiety chemically suitable for linking the epoxide group and the alkoxysilane group, and the modified cloned fragments are covalently bound to the surface;

wherein each array-bound cloned fragment has been mapped to a known location on the chromosome.

57. (original) A kit comprising an article of manufacture as set forth in claim 23 and printed matter, wherein the printed matter comprises instructions on hybridizing a sample of nucleic acid to an array-bound nucleic acid.

comprising

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- (a) providing a biological molecule;
- (b) providing a compound having the formula: $R_1 - X - R_2$, wherein R_1 comprises an amino group, R_2 comprises an alkoxysilane group soluble in solution and X comprises a moiety chemically suitable for linking the cyclic ether group or the amino group to the alkoxysilane group; and
- (c) reacting the biological molecule with the compound, thereby modifying the biological molecule with the compound.

83. (currently amended) A method for making an article of manufacture comprising an arrayed plurality of biological molecules covalently bound to a surface comprising

- (a) providing a biological molecule;
- (b) providing a compound having the formula: $R_1 - X - R_2$, wherein R_1 comprises a cyclic ether group or an amino group, R_2 comprises an alkoxysilane group soluble in solution and X comprises a moiety chemically suitable for linking the cyclic ether group or the amino group to the alkoxysilane group;
- (c) providing a surface comprising hydroxyl groups;
- (d) reacting the biological molecule with the compound, thereby modifying the biological molecule with the compound; and
- (e) depositing a plurality of modified biological molecules on the surface as discrete clusters, wherein a modified biological molecule is attached to the surface on at least one discrete and known location to form a cluster of substantially identical biological molecules and the array comprises a plurality of clusters.

84. (currently amended) A modified biological molecule comprising a biological molecule modified by reaction with a compound having the formula: $R_1 - X - R_2$, wherein R_1 comprises a cyclic ether group ~~or an amino group~~, R_2 comprises an alkoxysilane group and X comprises a moiety chemically suitable for linking the cyclic ether group ~~or the amino group~~ to the alkoxysilane group and the cyclic ether comprises an oxirane group, wherein the biological molecule is selected from the group of a nucleic acid or an analog or mimetic thereof, a polysaccharide or an analog or mimetic thereof, a lipid or an analog or mimetic thereof a

molecule modified by reaction with a compound having the formula: $R_1 - X - R_2$, wherein

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R_1 comprises a cyclic ether group or an amino group, R_2 comprises an alkoxy silane group and X comprises a moiety chemically suitable for linking the cyclic ether group or the amino group to the alkoxy silane group and the cyclic ether comprises a compound comprising an aromatic hydrocarbon epoxide group, wherein the biological molecule is selected from the group of a nucleic acid or an analog or mimetic thereof, a polysaccharide or an analog or mimetic thereof, a lipid or an analog or mimetic thereof, a peptidomimetic and a nonbiopolymeric small molecule.

86. (currently amended) A modified biological molecule comprising said biological molecule modified by reaction with a compound having the formula: $R_1 — X — R_2$, wherein R_1 comprises a cyclic ether group or an amino group, R_2 comprises an alkoxy silane group soluble in solution and X comprises a moiety chemically suitable for linking the cyclic ether group or the amino group to the alkoxy silane group and the R_1 group reacts with the biological molecule, wherein the biological molecule is selected from the group of a nucleic acid or an analog or mimetic thereof, a polysaccharide or an analog or mimetic thereof, a lipid or an analog or mimetic thereof, a peptidomimetic and a nonbiopolymeric small molecule.

87. (currently amended) A modified biological molecule comprising a biological molecule modified by reaction with a compound having the formula: $R_1 — X — R_2$, wherein R_1 comprises a cyclic ether group or an amino group, R_2 comprises an alkoxy silane group soluble in solution and X comprises a moiety chemically suitable for linking the cyclic ether group or the amino group to the alkoxy silane group and the R_1 group is covalently bound to the biological molecule, wherein the biological molecule is selected from the group of a nucleic acid or an analog or mimetic thereof, a polysaccharide or an analog or mimetic thereof, a lipid or an analog or mimetic thereof, a peptidomimetic and a nonbiopolymeric small molecule.

88. (currently amended) A modified biological molecule comprising a biological molecule modified by reaction with a compound having the formula: $R_1 — X — R_2$, wherein R_1 comprises a cyclic ether group or an amino group, R_2 comprises an alkoxy silane group soluble in solution and X comprises a moiety chemically suitable for linking the cyclic ether group or the amino group to the alkoxy silane group and the biological molecule comprises a nucleic acid or an analog or mimetic thereof.

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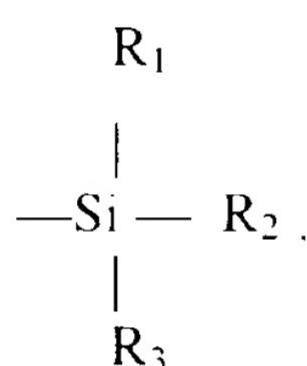
90. (previously added) The modified biological molecule of claim 88, wherein the nucleic acid reacts with the R₁ group at its 5' end.

91. (previously added) The modified biological molecule of claim 88, wherein the nucleic acid is an oligonucleotide.

92. (previously added) The modified biological molecule of claim 88, wherein the nucleic acid comprises a telomeric structure.

93. (previously added) The modified biological molecule of claim 88, wherein the nucleic acid comprises a chromatin structure.

94. (currently amended) A modified biological molecule comprising a biological molecule modified by reaction with a compound having the formula: $R_1 - X - R_2$, wherein R_1 comprises an amino group, R_2 comprises an alkoxy silane group and X comprises a moiety chemically suitable for linking the amino group to the alkoxy silane group and the alkoxy silane is selected from the group consisting of $-Si(OCH_3)_3$, $-Si(OC_2H_5)_3$ and



wherein R₁, R₂ and R₃ are selected from the group consisting of —H, —CH₃, —OCH₃, and —OC₂H₃₅, and provided that at least one of R₁, R₂ or R₃ is either —OCH₃ or —OC₂H₃₅.

95. (currently amended) A composition comprising a biological molecule modified by reaction with a compound having the formula: $R_1 - X - R_2$, wherein R_1 comprises an amino group, R_2 comprises an alkoxysilane group soluble in solution and X comprises a moiety chemically suitable for linking the amino group to the alkoxysilane group.

96. (previously added) The composition of claim 95, wherein the biological molecule comprises a polypeptide, a peptide or a peptidomimetic.

97. (previously added) The composition of claim 95, wherein the biological molecule

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99. (previously added) The composition of claim 95, wherein the biological molecule comprises a small molecule.

100. (previously added) The composition of claim 95, wherein the biological molecule comprises a nucleic acid or an analog or mimetic thereof.

101. (previously added) The composition of claim 100, wherein the nucleic acid comprises a DNA or an RNA.

102. (previously added) An article of manufacture comprising a plurality of biological molecules covalently bound to a surface, wherein, before attachment to the surface, the biological molecules are modified by reaction with a compound having the formula:

$R_1 - X - R_2$, wherein R_1 comprises an amino group, R_2 comprises an alkoxysilane group and X comprises a moiety chemically suitable for linking the amino group to the alkoxysilane group, and upon attachment to the surface the modified biological molecules are covalently bound to a surface.

103. (currently amended) A method for making an article of manufacture having biological molecules covalently bound to a surface, the method comprising

(a) providing each of a biological molecule; ~~(b)~~ providing a compound having the formula: $R_1 - X - R_2$, wherein R_1 comprises an amino group, R_2 comprises an alkoxysilane group and X comprises a moiety chemically suitable for linking the amino group to the alkoxysilane group; and ~~(c)~~ providing a surface comprising hydroxyl groups;

~~(b)-(d)~~ reacting the biological molecule with the compound, thereby modifying the biological molecule with the compound; and

~~(c)-(e)~~ depositing a plurality of modified biological molecules on a surface of the article of manufacture.